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May 14, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Re: International Conference on Harmonisation: Draft Guidance on E2E Pharmcovigilance Planning ("ICH-E2E") – Docket No. 2004D-0117- 69 Fed. Reg. 16579, March 30, 2004

To the U.S. Food and Drug Administration:

Thank you for providing an opportunity for consumer representatives and patient advocates to comment on the ICH-E2E draft guidance[1] that FDA and others would use to plan risk identification activities during postmarketing periods for drugs or biologics. The importance of followup risk identification is necessary to ensure the continuing safety and efficacy of approved medical products, including the potential HIV/AIDS global vaccine products currently in clinical trials with which I am concerned as a community advocate. From that perspective, I would like to offer two suggestions to clarify the description of pharmacovigilance tasks outlined in the ICH-E2E draft guidance. I request that FDA either discuss these issues with other members of the ICH and/or implement them when FDA considers the pharmacovigilance procedures that will apply in this jurisdiction.

Two Suggestions for ICH-E2E Implementation

1. Pharmacovigilance for long term risks

During clinical trial phases, informed consent documents may warn of long term or chronic risks that are not especially followed or measured by detailed adverse event reporting mechanisms. Many trials supporting licensing of medical products may not last long enough to collect hard data about theoretical long term risks or which can be sufficiently predicted by animal models. At the same time, such theoretical risks – however small they are thought to be - may be considered biologically possible by investigators or theoretically attributable to unknown elements in source biological materials. By exercising caution or perhaps because of liability concerns, nevertheless, participants are often warned of these long term risk possibilities such as potential cancers or prion related illnesses. From the point of view of the trial participant, it

[1] http://www.fda.gov/cber/gdlns/ichpvp.pdf . FDA has also recently published additional draft guidance for industry on Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment with a separate comment period. http://www.fda.gov/cber/gdlns/pharmacovig.pdf . These comments today are intended to address only the ICH-E2E document.

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would seem unfair to postulate such a risk without making subsequent effort to determine if the risks were genuinely part of the information set that supports a true consent.

During implementation of pharmacovigilance plans, FDA and others might consider reasonable means to identify the long term or chronic risks that are biologically plausible and mentioned in informed consent documents or processes. Improved pharmacovigilance plans would make genuine attempts to correlate followup safety monitoring with risks of which trial participants were told they should be aware. Otherwise, the risk warnings offered during informed consent would be seriously devalued.

2. Behavioral Risks

In the case of potential HIV/AIDS vaccines, some candidate interventions may be licensed that cannot provide substantial efficacy to prevent infection or full sterilizing immunity but can provide significant benefit to slow disease progression after infection. If that occurs, continued efficacy and safety issues will arise to monitor changing behavioral risks of vaccinated individuals to others and whether adequate counseling prepares vaccinees to understand the true benefits of those medical products. When designing appropriate pharmacovigilance plans for these and other medical products for which similar issues arise, procedures may include monitoring of continuing and changing behavioral risks. Evaluation of those risks could fall under pharmacovigilance methods described in the ICH-E2E draft guidance as a "drug utilization study."[2]

Thank you for considering these comments. I can be reached by telephone at 415/268-7469 or by email at rreinhar@mofo.com.

Sincerely,

Robert Reinhard

Robert Reinhard
Community Advisory Board Member,
HIV Vaccine Trials Network

[2] Ibid., Annex, p. 14.